Major Kidney Clinical Research Studies and Projects Inventory*

Improving Outcomes in Diabetic Nephropathy

1. Administrative Data

(a) Name of study/research project and acronym:

Improving Outcomes in Diabetic Nephropathy

(b) Type of study/research project (randomized clinical trial, epidemiological study, database, etc.):

Randomized clinical trial

(c) Funding status (currently funded, study/project completed):

Actively funded in progress

(e) Recruitment status (recruitment completed, currently recruiting):

Recruitment in early stages

(f) For studies/project currently recruiting, indicate total sample size or number currently enrolled and anticipated period of recruitment:

Sample size 72; 0 enrolled; recruitment period 1 year

(g) Data coordinating center principal investigator contact information (mailing address, phone, fax, e-mail address):

None

(h) Number of recruiting sites, list of principal investigators at recruiting sites, and contact information as in (f) above:

Two sites in Dallas

(i) List of principal investigators at central laboratories/facilities (identify type of central facility) and contact information as in (f) and (g) above:

Robert D. Toto

(j) Roster of Data and Safety Monitoring Board/Scientific Advisory Committee or other oversight committee(s):

Ronald Victor, Chairman
Beverley Huet
Khashayar Sakhaee
Richard Auchus

(k) Private sector support (type of support, e.g., financial, donation of drugs/placebo, etc.):

None at this time

2. Study Design (for completed studies, a copy of the primary publication can substitute for information below)

(a) Objective**:**

Determine whether ACEi add on therapies including ARB and mineralocorticoid receptor antagonists reduce proteinuria in diabetics with nephropathy

(b) Study design:

Double-blind randomized placebo-controlled trial

(c) Major inclusion criteria:

- Type 1 or young type 2 diabetics
- Albumin/creatinine ratio > 300 mg/g
- Systolic BP > 130 mmHg

(d) Major exclusion criteria:

- Baseline serum creatinine > 3.0 mg/dl in females and 3.5 mg/dl in males or glomerular filtration rate $\leq$ 20 ml/min estimated by the MDRD equation
- Males with gynecomastia or evidence of hypogonadism.
- Serum potassium concentration $\geq$ 5.0 mEq/L on ACE inhibitor therapy
- Medical need for ongoing calcium channel blocker therapy
- Glycated hemoglobin level > 11 mg/dl
- Chronic daily use of non-steroidal anti-inflammatory agents

- BMI > 40 kg/m2
- Stroke or myocardial infarction within the preceding 12 months prior to randomization
- Coronary revascularization procedure within past 6 months
- Clinically apparent congestive heart failure defined as clinical signs of heart failure or an ejection fraction of < 40% (and/or depressed LV systolic function by echocardiogram).
- Renal disease known or in the opinion of the investigator caused by a condition other than diabetes
- Pregnancy (pre-menopausal women, i.e. those of child-bearing potential, may participate if birth control method is in use throughout the study)

(e) Description of the intervention(s):

Add on spironoloactone 25 mg per day or losartan 100 mg per day to ramipril 40 mg per day

(f) Baseline/eligibility visit schedule (number of visits, major assessments):

Screening visit 1; Run-in visit 3-6

(g) Follow-up contact schedule (frequency, type of visit/phone, in-clinic, major assessments):

Clinic visit monthly for 12 months

(h) Primary outcome, secondary outcomes:

Primary: 40% reduction in baseline urine albumin/creatinine ratio

Secondary: (a) serum potassium and creatinine to assess safety, (b) TGF-□, the latter as a surrogate marker for ongoing renal injury, (c) plasma renin activity, angiotensin II and aldosterone levels, and (d) plasma lipids and lipoprotein composition

(i) Brief summary of power estimates used to justify sample size/duration, including critical assumptions (i.e., effect-size estimates, estimated event rates, or rate of change in outcome measure):

The sample size is calculated to have sufficient power to detect differences between the placebo and active treatment (losartan or spironolactone) groups. The expected difference (% change) in response between groups in the albumin/creatinine ratio is 40%. The estimate of the variability of the change in albumin/creatinine ratio is 40%-45% (CV%) with an alpha 0.05 and a beta of 0.8. The 40% effect size in reduction in albumin/creatinine ratio from baseline is based on previous publications by my laboratory and others. Review of the literature in both type 1 and type 2 diabetics and non-diabetics with proteinuric nephropathies indicates that ARBs generally reduce albuminuria by 30%-50% after 1 or more months of treatment. In addition, mean reduction in proteinuria after add-on of either an ARB or spironolactone to ACEi are in the range of 40%-50% nephropathies.

(j) Web site:

Under construction

3. Data and Biological Sample Resources

(a) Biological samples collected in ongoing studies/research projects (specify the type of sample, e.g., blood, urine, etc., the amount, and the point in the study when samples were collected, e.g., baseline visit #1, baseline visit #2, follow-up visit #1; specify months after randomization/study entry):

Blood samples for renal function and biochemistry monthly, urine protein, and GFR estimate measured quarterly

(b) Biological samples currently in storage from completed trials (grid showing sample collection time, type of sample, amount, and number of study participants sample was collected from, and physical location of where the samples are stored):

N/A

(c) Brief summary of typical informed consent provisions (template informed consent form acceptable), including major variables in participant consents, if applicable. For example, “use for other studies or not”, “allow genetic studies or not.”) Does consent include use of samples in other studies that are not part of the main study?

(d) Data collected (grid of data collection by time/clinic visit with specificity on the type of information collected, e.g. quality of life with SF-MOS 36, measurement of kidney function by GFR, serum creatinine measurement, etc.):

Data collection: clinic and ambulatory blood pressure, glomerular filtration rate, plasma renin and aldosterone level, urine TGF-beta, kidney function, protein excretion, adverse event collection.

(e) Any provisions for distributing resources outside of the study? What is the sharing plan?

None

4. Ancillary Studies

(a) Process and contact person (name, address, phone, fax, and e-mail address) for application to perform ancillary studies:

N/A

(b) List of ancillary studies approved, completed and ongoing (including source of funding and amount):

N/A

5. List of Publications and Presentations (full citations, also note manuscripts in progress)

None

***Cooperative Agreement, Contract, and Selected Investigator-Initiated NIDDK-Supported Studies**